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1: Eur J Pharmacol. 1999 Aug 27;379(2-3):125-33. Related Articles, Links

Reboxetine attenuates forced swim test-induced behavioural and neurochemical alterations in the rat.

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The forced swim test is a behavioural paradigm that is predicative of antidepressant activity in rodents. Until recently, research has focused on the ability of antidepressant drugs to decrease immobility in the forced swim test paradigm, but the neurochemical sequelae induced by swim stress, or the neurochemical basis of antidepressant-induced behavioural changes have received little attention. In this regard, we have recently demonstrated that forced swim test exposure increases serotonergic activity in the amygdala, frontal cortex and hippocampus and dopamine turnover in the striatum. In addition, forced swim test-exposure activates the hypothalamic pituitary adrenal axis. The purpose of the present study was to examine the effect of treatment with the selective noradrenaline reuptake inhibitor reboxetine (3, 10 and 30 mg/kg; i.p.) on immobility and defaecation scores in the forced swim test, and on forced swim test-induced neurochemical and hypothalamic pituitary adrenal axis changes in the rat. Reboxetine treatment (10 and 30 mg/kg) significantly decreased immobility and defaecation in the forced swim test in dose dependent manner. Furthermore, reboxetine produced a dose dependent attenuation of forced swim test-induced increases in serotonin turnover in the amygdala and frontal cortex and dopamine turnover in the striatum. Reboxetine (30 mg/kg) produced a modest, but non-significant, attenuation of forced swim test-induced increases in serum corticosterone concentrations. These data demonstrate that, in addition to the behavioural activity of reboxetine in the rat forced swim test paradigm, a dose-dependent attenuation of swim stress-induced increases in serotonergic and dopaminergic activity occurred in a region specific manner. These are the first data to demonstrate that treatment with the selective noradrenaline reuptake inhibitor, reboxetine can impact on the activity of other neurotransmitter systems in response to stress. Moreover, these data further demonstrate that this paradigm is a valuable tool in studying the effect of antidepressants, on both behaviour and swim stress-related alterations in central neurotransmitter function and hypothalamic pituitary adrenal axis activity in the rat.

Antidepressants for the new millennium

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ABSTRACT

Despite a remarkable structural diversity, most conventional antidepressants may be viewed as 'monoamine based', increasing the synaptic availability of serotonin, norepinephrine, and/or dopamine. Both preclinical and recent clinical studies indicate that compounds which reduce transmission at N-methyl-D-aspartate (NMDA) receptors are antidepressant. Moreover, chronic administration of antidepressants to mice alters both the mRNA levels encoding N-methyl-D-aspartate receptor subunits and radioligand binding to these receptors within circumscribed areas of the central nervous system. It is hypothesized that these two different treatment strategies converge to produce an identical functional endpoint: a region-specific dampening of NMDA receptor function. The pathways leading to this convergence provide a rudimentary framework for discovering novel antidepressants.